# METHODS OF PREPARING SUBSTITUTED TETRACYCLINES WITH TRANSITION METAL-BASED CHEMISTRIES

## ABSTRACT OF THE DISCLOSURE

The present invention relates to novel chemistries which allow for heretofore unobtainable substituted tetracycline compounds which exhibit significant antibacterial activity. The methods disclosed herein utilize reactive tetracycline-based precursor compounds, reactive organic substituent precursors and transition metal catalysts under conditions such that a tetracycline compound substituted with the desired organic substituent is formed. In one embodiment of the invention, a substituted tetracycline compound may be prepared by combining a reactive tetracycline-based precursor compound such as an arene tetracycline diazonium salt, and a reactive organic substituent precursor, e.g., alkenes, substituted alkenes, vinyl monomers, aromatics and heteroaromatics, in the presence of a transition metal catalyst, such as palladium chloride, under conditions such that a tetracycline compound substituted with the organic substituent is formed. Such compounds may optionally act as intermediates for making other compounds, e.g., hydrogenation of unsaturated groups on the substituent.